

CLAIMS

1. Chromatography process in which a particulate medium is packed into a bed space of a column housing to form a close-packed bed filling the bed space and a process liquid containing components to be separated is passed through the packed bed to separate the components, characterised by transmitting an ultrasound signal through the bed space and detecting the transmitted signal to determine a state or position of said particulate medium in the bed space.
2. Chromatography process according to claim 1 comprising monitoring the speed of transmission of the ultrasound signal through the bed space.
3. Chromatography process according to claim 1 or 2 comprising monitoring the attenuation of the transmitted signal.
4. Chromatography process according to any one of the preceding claims comprising said ultrasound signal transmission through the bed space during packing of the particulate medium into the bed space via a port in the wall of the column housing, as a pumped slurry.
5. Chromatography process according to claim 4 in which one or both of packing pump pressure and particulate medium slurry concentration is/are controlled in dependence on the packing status determined from the ultrasound signal detection.
- Sub P1

Sub A2

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6. Chromatography process according to claim 4 or 5 in which detected ultrasound signals are transmitted transversely to the direction of accumulation of the packed bed of medium.

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7. Chromatography process according to any one of claims 4 to 6 in which detected ultrasound signals are transmitted through the bed space at plural locations distributed along the direction of accumulation of the packed bed of medium.

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8. Chromatography process according to claim 7 in which a real-time rate of advance of the front of the accumulating bed, determined from its detected passage past plural locations as mentioned, is compared with a predetermined target rate of advance value and the packing pump pressure and/or slurry concentration adjusted as necessary.

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Sub A3

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9. Chromatography process according to claim 7 or 8 in which respective real-time rates of advance are determined for a plurality of said locations and compared with respective target values constituting a predetermined packing profile, and feedback control signals sent to a packing pump in dependence on the comparisons.

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10. Chromatography process according to claim 9 in which said predetermined packing profile prescribes an initial phase with a slower rate of advance than in a subsequent main phase.

Sub A4
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11. Chromatography process according to any one of claims 4 to 10 in which a control processor, operatively connected to the packing pump and ultrasound detection arrangement, is loaded with target packing data from a discrete data carrier, and controls the packing pump in dependence on comparisons between the detected and target data.
- 10 12. Chromatography process according to any one of claims 4 to 11 in which a detected ultrasound transmission adjacent that end of the bed space last filled by the accumulating bed is used to detect the arrival of the advancing bed front and thereby initiate reduction or cessation of pump operation at the end of
- 15 the packing procedure.
13. Chromatography process according to any one of claims 4 to 12 in which a control processor is programmed to respond to a detected dip in packing pressure,
- 20 corresponding to the bed space becoming full of medium, by turning off the packing pump.
14. Chromatography process according to any one of the preceding claims comprising said ultrasound transmission
- 25 through the bed space during the passage of process liquid through the packed bed, to detect the presence and/or position of a said component in or passing through the bed.
- 30 15. Chromatography process according to claim 14 in which detected ultrasound transmissions at plural locations along the packed bed are used to track the

progress of a band of a said component passing through the bed.

Sub 145 16. ~~Chromatography process according to any one of the preceding claims in which a detected ultrasound transmission through the packed bed adjacent an input end for the process liquid is used to determine the extent of encroachment of bound impurity into the bed from the input end.~~

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~~17. Chromatography process according to any one of the preceding claims, carried out using apparatus according to any one of the following claims.~~

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18. Chromatography apparatus comprising a chromatography column having a housing wall with side wall and end wall portions defining an internal bed space for containing a particulate packing medium, characterised by at least one ultrasound transmitter on the housing wall, disposed to transmit an ultrasound signal through the bed space, and a detector to detect the transmitted signal.

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19. Chromatography apparatus according to claim 18 in which at least one said ultrasound transmitter is comprised in a transceiver unit also comprising a said detector.

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Sub 146 20. ~~Chromatography apparatus according to claim 18 or 19 in which said transmitter and/or detector is on the outside of the housing wall, so that the ultrasound signal is transmitted to the detector through the wall as well as through the bed space.~~

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21. Chromatography apparatus according to any one of claims 18 to 20 in which plural said transmitters and/or plural said detectors therefor are distributed along the column in a direction between an inlet and an outlet of the column.

22. Chromatography apparatus according to any one of claims 18 to 21 in which the column is a vertical cylinder, e.g. with a steel side wall.

23. Chromatography apparatus according to any one of claims 18 to 22 comprising a control processor operatively connected to the ultrasound transmitter and detector and programmed to determine a speed and/or attenuation for the transmissions between them via the internal bed space.

24. Chromatography apparatus according to any one of claims 18 to 23 in which the chromatography column has a port through its housing wall adapted for the injection of a slurry of particulate medium for packing the column.

25. Chromatography apparatus according to claim 24 in which plural said transmitters and/or plural said detectors are distributed along the column to enable detection of ultrasound transmissions along a corresponding plurality of paths through the internal bed space.

26. Chromatography apparatus according to claim 25 in which a control processor is operatively connected to the transmitters and detectors and programmed to determine,

for said plurality of transmission paths, respective transmission speeds and/or attenuations.

27. Chromatography apparatus according to claim 26 in
5 which the control processor is programmed to detect successive positions of the front of an accumulating packed medium bed in the column by means of the change in transmission characteristics as the front crosses respective transmission paths, and to
10 determine a real-time rate of advance for said front;
compare the real-time rate of advance with a target rate of advance predetermined for the corresponding position on the column or stage of the process, and
15 generate a control signal to control a packing pump in dependence on the comparison.

28. Chromatography apparatus according to claim 27 in
20 which the control processor has a data reader for reading a set of target data for the packing procedure, appropriate to the column and medium being packed, from a discrete data carrier.

29. Chromatography packing apparatus for use in packing
25 a particulate medium into a chromatography column having a column wall having a housing wall with side wall and end wall portions defining an internal bed space, with a packing port through the housing wall for introduction of a slurry of the particulate medium in a carrier liquid;
30 the apparatus comprising a motorised pump for pumping the slurry to the packing port and a control processor connected to control the output of the pump, the control processor having one or more inputs to

receive the detected signals from one or more detectors for ultrasound transmissions and being programmed to adjust the output of the pump in dependence on detected signals.

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30. Chromatography packing apparatus according to claim 29 in which the control processor is programmed to determine an advance rate based on the time elapsing between signals from two different ultrasound transmitter/detector combinations indicating a change to greater attenuation or greater speed of the respective transmissions, to compare the advance rate with a predetermined target value and to send a signal to increase, maintain or decrease the pump output according to whether the predetermined rate is less than, corresponds to or is greater than the predetermined target value.
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- 29 *Sub H* 31. ~~Chromatography packing apparatus according to claim 29 or 30 comprising a set of the ultrasonic transmitters and detectors.~~

- 25 32. ~~Chromatography packing apparatus according to any one of claims 29 to 31 comprising a data reader for reading a set of prescribed packing parameters for a given column and medium from a discrete data carrier.~~